present Office Action includes rejections under 35 U.S.C. §103 and an objection to the declaration under 37 C.F.R. §1.175, which are discussed below.

The Office Action states that the declaration filed with this reissue application is allegedly "defective" under 37 C.F.R. §1.175 because Applicants' statement that they erred in not claiming the chemical compounds set forth in claims 9-26 was not accompanied by a "rationale stating how not claiming the compounds is an error." *See* Office Action dated November 6, 2001, page 3. Applicants respectfully assert, however, that such a statement is not necessary inasmuch as the failure to claim that to which the Applicants were entitled itself constitutes an error rectifiable by reissue. Indeed, 37 C.F.R. §1.175(a)(1) recognizes that a statement to this effect is all that is required:

> (a) The reissue oath or declaration in addition to complying with the requirements of §1.63, must also state that:
>
> (1) The applicant believes the original patent to be wholly or partly inoperative or invalid by reason of a defective specification or drawing, ***or by reason of the patentee claiming more or less that the patentee had a right to claim in the patent***, stating at least one error being relied upon as the basis for the reissue...

37 C.F.R. §1.175(a)(1). [1]

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[1]Applicants note that the outstanding rejection with respect to the declaration differs from that recited in the prior Office Action. For example, the prior rejection was based on an alleged absence of a statement regarding errors in the claims, whereas the present rejection is based on the alleged insufficiency of the statement that the Examiner had mistakenly alleged to be missing. This new ground of rejection calls into question designation of the present Office Action as "final."

As is clear from the above passage, the inventor's statement that they claimed less than that to which they were entitled to claim consitutes "at least one error being relied upon as the basis for the reissue." Accordingly, Applicants respectfully submit that the declaration is proper and respectfully request that the objection thereto be reconsidered and withdrawn.

Claims 9-19 stand rejected under 35 U.S.C. §103 as allegedly being obvious in view of Montgomery, et al., *J. Med. Chem.*, 29, 2389-2392 (1986) (the Montgomery reference) or Perlman, et al., *J. Med. Chem.*, 28, 741-748 (1985) (the Perlman reference) when taken in view of either Gait, *Oligonucleotide Synthesis: A practical approach*, IRL Press Limited (1984) (the Gait reference) or Greene, et al., *Protective Groups in Organic Chemistry*, pp. 413-416 (1991) (the Greene reference). As best understood, the Office Action asserts that, depending upon the involved claim, either the Perlman or Montgomery reference teaches the general purine or pyrimidine formula of the claimed compounds, respectively, and the Gait or Greene references (sometimes both are necessary) teach the particular protecting groups thereon.

As a threshold matter, Applicants note that although the Office Action states that the Montgomery reference teaches the 2-deoxy-2-fluoro-β-D-arabinofuranosyl compounds set forth in claims 9-19 wherein the base is "purine," the Montgomery reference fails to teach, *inter alia*, the base adenine. Thus, it could not have been "obvious" to use a protecting group appearing, for example, in the Gait or Greene references in connection with such a compound, because the core compound is not described in the primary reference. Accordingly, Applicants respectfully submit that the rejection with respect to claims 11, 14, and 18 is misplaced and should be

withdrawn.

With respect to the remaining claims, Applicants note that the Office Action admits that neither the Montgomery nor Perlman reference teaches compounds containing the protecting groups recited in the claims. Moreover, the Office Action admits that, for several claims, it is necessary to combine more than two references to arrive at the claimed subject matter. Nevertheless, the Office Action asserts that one of skill in the art would have been motivated to use known protecting agents given the alleged use of such groups in oligonucleotide synthesis. *See* Office Action dated November 6, 2001, page 4.

Applicants respectfully submit, however, that the proper standard is not whether the invention is obvious once the combination is made, but rather, without the benefit of hindsight, whether the art suggested the desirability of the combination itself. *See In re Gordon*, 733 F.2d 900, 902, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984). Using Applicants' disclosure as a blueprint to reconstruct the claimed invention from isolated pieces of the prior art contravenes the statutory mandate of section 103 that obviousness be assessed at the point in time when the invention was made. *Grain Processing Corp. v. American Maize-Prods. Co.*, 840 F.2d 902, 907, 5 U.S.P.Q.2d 1788, 1792 (Fed. Cir. 1988). Accordingly, even if the art cited in the Office Action could have been modified to produce the claimed invention, this fact alone would not have made the modification obvious. *In re Laskowski*, 871 F.2d 115, 117 (Fed. Cir. 1989). The art must still suggest the desirability of the modification. *Id.*

Applying these tenets to the present situation, it is only possible to construct the claimed

subject matter by culling various moieties from the prior art, in certain cases, from more than two references. For example, claims 16 and 17 recite 2-deoxy-2-fluoro-β-D-arabinofuranosyl compounds wherein the base is protected by isobutyryl and benzoyl, respectively, and R^1 is protected by t-butyldimethylsilyl. The Office Action admits that both the Gait reference and the Greene reference would have had to be combined to teach the claimed subject matter, namely, the use of isobutyryl and benzoyl groups for the protection of exocylic amines and the use of t-butyldimethylsilyl for the protection of the hydroxyl group. Applicants respectfully submit that the requisite prior art suggestion to combine references becomes less plausible when the necessary elements are found in an increasing number of references. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986).

In any case, none of the cited prior art addresses the fundamental failure of these references to provide a motivation to teach the desirability of combining the references, *i.e.*, to use the protecting groups of these secondary references in connection with the arabinofuranosyl compounds of the Montgomery and Perlman references. In fact, Applicants respectfully submit that neither the Montgomery nor Perlman references even suggest the use of protecting groups on the compounds described therein. Thus, absent a compelling reason as to why the skilled artisan would have been motivated to make the modifications proposed in the Office Action, Applicants respectfully submit that the rejection claims 9-19 under 35 U.S.C. §103(a) should be withdrawn.

Claims 20-26 remain rejected under 35 U.S.C. §103 as allegedly being unpatentable over the Gait reference in view of Sterzycki et al., European Patent Application No. EP 0316017 (the

Sterzycki reference). In this regard, the Office Action asserts that it would have been obvious to prepare oligonucleotides from the arabinonucleosides of the Sterzycki reference, according to the methods taught in the Gait reference, for the purpose of constructing, selecting, and determining DNA sequence recombinants or conducting site directed mutagenesis. According to the Office Action, the motivation to do so is provided by Chapter 4 of the Gait reference, authored by Sproat et al., entitled "Solid-phase Synthesis of Oligodeoxyribonucleotides by the Phosphotriester Method" (the Sproat reference).

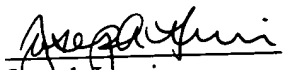
In the Reply filed March 29, 2001, Applicants asserted that the Office Action failed to identify a credible, motivational force that would have impelled the skilled artisan to modify the disclosure of the Sproat reference to provide an oligonucleotide comprised of the nucleosides of the Sterzycki reference. Specifically, Applicants asserted that the motivation that was purported in the Office Action (*i.e.*, to construct, select, and determine DNA sequence recombinants or, alternatively, for use in site directed mutagenesis) was not credible because (1) an oligonucleotide built from the nucleosides of the Sterzycki according to the teachings of the Sproat reference would not, in fact, produce DNA; and (2) the resultant compounds would be ill-suited for site directed mutagenesis because a naturally-occurring nucleic acid is required for such a use. *See* Applicants Reply, page 9.

The present Office Action now mistakenly asserts that because the Applicants refer to the Sproat reference in their own specification, Applicants are "questioning the credibility of the same reference it relies upon to make the claimed oligonucleotides." *See* Office Action dated

November 6, 2001, page 5. The teachings of the Sproat reference *for the purpose of constructing oligonucleotide*s is not in question. What is in question is why the skilled artisan would have been motivated to use the teachings of the Sproat reference in combination with the Sterzycki reference to construct the claimed compounds in the first place. Significantly, the Office Action does not provide a compelling reason in either the Sproat or the Sterzycki reference for doing so. Under such circumstances, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 20-26 under 35 U.S.C. §103.

Applicant believe the foregoing constitutes a complete response to the Office Action of record and submit that all pending claims are in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,



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